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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/754,457	KODADEK, THOMAS	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27,44 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27, 44-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 15-18 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430.

Dower et al. teach that when using random peptide generation systems that allow for multivalent ligand-receptor interaction, one must recognize that the density of the immobilized receptor is an important factor in determining the affinity of the ligands that can bind to the immobilized receptor. At higher receptor densities (e.g., each anti-receptor antibody-coated well treated with 0.25 to 0.5 mg of receptor), multivalent binding is more likely to occur than at lower receptor densities (e.g., each anti-receptor antibody-coated well treated with 0.5 to 1 ng of the receptor), If multivalent binding is occurring, then one will be more likely to isolate ligands with relatively lower affinity, unless one uses high densities of immobilized receptor to identify lead compounds and uses lower receptor densities to isolate higher affinity derivative compounds (col. 13, lines 25-38.) In short Dower et al. teach that for multivalent ligand-receptor interaction, using higher receptor densities will increase the likelihood of multivalent binding than at lower receptor densities, which thus increases

the likelihood of isolating ligands with relatively lower affinity. It is understood that the multivalent ligand-receptor interaction relates to the target ligand binding to multiple receptors. Dower et al. emphasizes that the multivalent binding permits the detection of binding events of low intrinsic affinity (col. 33, lines 42-55.)

It is noted that Applicant's claim recites a "composition" but it appears that this term is used to refer to what is generally understood to be an article since the claimed invention includes a surface, i.e., binding elements on a surface.

It is also noted that Applicant's invention is based on the discovery that high density will increase the likelihood of the multivalent binding between receptors and the target 'as some fraction of the possible pairs of molecules on the surface will have an appropriate geometry relative to one another to bind the target molecule" (page 4, lines 23-27.) Such discovery is also disclosed by Dower et al. (col. 13, lines 25-38.)

As to claims 1 and 2, Dower et al. disclose comcomitant binding of a target molecule to two or more binding elements on a surface (col. 13, lines 25-38 and col. 33, lines 42-55). It appears that on page 4, lines 20-21 Applicant provides a precise definition for "low to modest affinity" as an equilibrium dissociation constant between 10^{-3} M to 10^{-8} M. Thus the term "low-to-moderate affinity" in Applicant's claims will be interpreted based on this definition. While Dower et al. use the term "relatively lower affinity" but does not provide a definition or example, Dower et al. nevertheless provides a general disclosure regarding multivalent bonding between the target ligand and multiple receptors as discussed above. Given the general teachings of Dower et al., the skilled artisan would have utilized this knowledge for binding various desired

targets using various respective receptors, including peptides (Dower et al. disclose antibody as an example) including binding receptors having low affinity as defined by Applicant, i.e., those having an equilibrium dissociation constant between 10^{-3} M to 10^{-8} M. Such binding by definition results in a high affinity interaction.

As to claim 4, the antibody on the support inherently has more than one binding element.

As to claim 5, since Applicant has not recited further description of the spacer, the antibody on the support inherently includes what is considered a spacer operatively coupled to the first binding element, the second binding element or both the first and second binding element. (It is also noted that Dower et al. disclose that compounds may also include spacers or linkers in cases where the compounds are to be attached to a solid support.(col. 28, lines 4—42.)

As to claim 15, the sample is a cell lysate (col. 33, lines 13 -16.)

As to claim 16, Dower discloses that immobilized materials may be labeled to provide a detectable signal for medical research and diagnostic uses (col. 28, lines 47-52.)

As to claims 17,18, 44, the first target molecule is a biological molecule, e.g., thrombopoietin receptor, TPO-R (28, 43-47), which is a polypeptide.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430, in view of Bellet et al., 5,011,771.

Dower et al. disclose the invention substantially as claimed (see above) except for the plurality of binding elements comprising at least a first and a second binding element having distinct binding specificity for a target molecule as compared to each other.

However, multivalent targets having different epitopes for different binding partners and that allow for simultaneous binding to the binding partners are known in the art, as illustrated by Bellet et al. in disclosing assays for multivalent antigens that have binding sites for at least two antibodies each against a different epitope on the antigen (col. 2, lines 44-52) wherein the epitopes are sufficiently separated from one another so as to allow simultaneous binding of a different immobilized antibody to each of the epitopes (col. 8, lines 45-61.) It would have been obvious to one of ordinary skills in the art to utilize different binding partners (equivalent to Applicant's binding elements) for simultaneous binding to the target in the invention disclosed by Dower et al. in the case in which the tartget is multivalent and has different epitopes for different binding partners, since the skilled artisan would have recognized that the same principle disclosed by Dower et al, that is, using high receptor densities to increase the likelihood of multivalent binding of a molecule to the immobilized receptors, applies also in the case in which the multivalent target molecule has different epitopes for different binding partners, such molecules being disclosed by Bellet et al.

Claims 6, 7, 8, 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430, in view of Ring, 5,705,614, and further in view of Bellet et al., 5,011,771

Dower et al. discloses the invention substantially as claimed (see above) except for the plurality of binding elements comprising at least a first and a second binding element having distinct binding specificity for a target molecule as compared to each other (as recited in claim 3), or wherein the second binding element is an oligomer or peptide (as recited in claims 6 and 7)

However, Ring teaches that bispecific oligomers may be made by linking two different entities that have been digested. More specifically, Ring teaches that bispecific antibodies are generally obtained in one of two ways: (1) generation by chemical linkage; or (2) production by engineered cell lines. Chemical linkage involves the linking of either two entire monoclonal or polyclonal antibodies, or antigen-specific fragments thereof. Two such entities having different specificities are linked using a chemical crosslinking agent conventional in the art. Alternatively, each antibody may be digested to produce F(ab')2 fragments, which may then be reduced to produce individual Fab' fragments. One Fab' fragment may then be derivatized with a reagent and then reacted with the second Fab' fragment of different specificity to regenerate a linkage at the hinge region and create a bispecific F(ab')2 fragment, which is referred to as a heterodimer or oligomer (col. 9, col. 33-60.)

Moreover, Bellet et al. teach that multivalent targets having different epitopes for different binding partners allow for simultaneous binding to the binding partners are known in the art. Bellet et al. in discloses assays for multivalent antigens that have binding sites for at least two antibodies each against a different epitope on the antigen (col. 2, lines 44-52) wherein the epitopes are sufficiently separated from one another so as to allow simultaneous binding of a different immobilized antibody to each of the epitopes (col. 8, lines 45-61.) It would have been within the skills of the ordinary artisan at the time the invention was made to utilize the Bellet et al. and Ring teachings to modify the Dower et al. invention such that the binding elements for the target have distinct binding specificity by using the chemistries as taught by Ring in a configuration that allows for the simultaneous binding of the two binding elements to the target, as taught by Bellet et al.

As to claim 6, the binding element is therefore also an oligomer.

As to claim 7, the oligomer is a peptide or peptide derivative (since it is digested from an antibody.)

As to claim 8, the peptide derivative is comprised of one or more non-natural amino acid (since it is synthetically derived.)

As to claim 10, the first binding element is thus also a peptide.

As to claims 11, 12 and 13, while Ring does not teach that the first binding element is operatively coupled to a terminal monomer of the oligomer, or an internal monomer of the oligomer, or that there is a plurality of first binding elements are operatively coupled to the oligomer, such chemistries would have been within the skills

of the ordinary artisan given the teachings of Ring regarding use of various known cross-linkers to link various digested fragments as desired.

Claims 9 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430, in view of Liotta et al. 6,153,596.

Dower et al. discloses the invention substantially as claimed (see above) except for the peptide derivative comprising one or more peptoid monomers (which is defined by Applicant in the specification as N-substituted oligoglycines.)

As to claim 9, Liotta et al. however teach that peptoids, i.e., N-substituted oligoglycines, have been considered for the development of pharmaceuticals. Peptoid libraries, prepared by combinatorial synthesis have been screened for peptoids having biological function. Such libraries have, for example, been screened for peptoids with affinity for binding to ligands. Liotta et al. also cite prior art that discloses a method for generating and screening peptoid libraries to isolate peptoids that bind to protein or peptide receptors. Liotta et al. also disclose that conjugates of selected peptoids can also be made (col. 7, lines 23-51.) It would have been obvious to the skilled artisan to utilize the Dower et al. teachings to screen for peptoids with affinity for binding to ligands as taught by Liotta et al. for development of pharmaceuticals.

As to claim 45, the peptoid is also a peptide-like molecule.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., ,6,465,430, in view of Schwartz, 6,800,728.

Dower et al. discloses the invention substantially as claimed (see above) except for the support being a chemically-modified glass slide.

However Schwartz disclose solid supports, including beads or glass slides that have been modified by reaction with a bifunctional reagent. The modified solid supports are useful in immobilization of biomolecules for diagnostic applications (col. 3, line 60 – col. 4, line 3.) Schwartz also disclose the use of such modified slides to prepare microarrays of biomolecules (col. 20, line 54 – col. 21, line 14.)

While Dower et al. disclose immobilized binding elements but do not disclose the details of how the binding elements are immobilized, in particular that the solid support is a chemically-modified glass slide, the skilled artisan would have looked to the art for immobilization techniques and various types of appropriate solid supports, such as the Schwartz chemically-modified glass slide.

Claims 19, 20, 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430, in view of Chin et al., 6,197,599 .

Dower et al. disclose the invention substantially as claimed (see above), except for the first target molecule being a modified polypeptide (as recite in claim 19), or

wherein the modification is phosphorylation, or ubiquitylation (as recited in claim 20).

Chin et al. however teach that protein posttranslational modifications (e.g., phosphorylation, glycosylation, and ubiquitination) play critical roles in regulating protein activity and that simultaneously detecting and identifying multiple phosphorylated proteins is highly desirable for signal transduction studies and clinical diagnosis (col. 2, lines 4-21.)

Chin et al. teach that protein array allows rapid detection of many proteins and thus makes it possible to compare protein expression profiles from different sources or those from the same source but under different conditions. Information on protein expression profile is very useful in identifying diagnostic and therapeutic targets. Protein array also makes it possible to detect posttranslational modifications of numerous proteins and provide a valuable tool to investigate protein and cellular regulations. Moreover, protein arrays can screen a large number of potential interactions directly; and it can detect interactions that take place only under certain conditions, e.g., phosphorylation.

It is further disclosed that in order to reveal the broad protein expression pattern in a source (e.g. a cell line), thousands of different antibodies are immobilized in a single support. The number of different agents immobilized on one solid support varies depending on the particular applications (col. 4, lines 40-53.) The proteins in the samples can be labeled, and after removing unbound material, the proteins are detected. Because the antibodies are immobilized in a predetermined order, the identity of the protein captured at each position is therefore known (4, 54- col. 5, line

17.) Phosphorylation or ubiquitination can be identified using specific antibodies (col.5, lines 17-38, col. 7, lines 8-32.) Many proteins can be simultaneously examined with an array comprising a large umber of immobilized antibodies (col. 6, line 46 – col. 7, line 5.)

As to claims 19 and 20, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the assay teachings generally disclosed by Dower et al. to detect modifications such as phosphorylation or ubiquitination as taught by Chin et al. by using the appropriate chemistries known, since Chin et al. teach that such modifications are useful in identifying diagnostic and therapeutic targets.

As to claim 22, it modifying the Dower et al. teachings to simultaneously detect multiple targets, as suggested by Chin et al., the skilled artisan would utilize a different set of binding elements for the second target. This different set of binding elements is equivalent to the claimed "third and fourth low-to-moderate binding element".

Claims 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430, in view of Ring, 5,705,614, and Bellet et al., 5,011,771, and further in view of Chin et al., 6,197,599.

Dower et al. discloses the invention substantially as claimed (see above) except for third and fourth binding elements being distinct from each other (as recited in claim

23), or the third and fourth binding elements having distinct binding specificity as compared to the first and second low affinity binding elements (as recited in claim 24), or the first and second low affinity binding elements being segregated from the third and fourth low affinity binding elements on the solid support (as recited in claims 25-26.)

As to the limitations regarding a third and fourth binding elements being distinct from each other, Ring and Bellet et al. suggest such modifications.

Ring teaches that bispecific oligomers may be made by linking two different entities that have been digested. More specifically, Ring teaches that bispecific antibodies are generally obtained in one of two ways: (1) generation by chemical linkage; or (2) production by engineered cell lines. Chemical linkage involves the linking of either two entire monoclonal or polyclonal antibodies, or antigen-specific fragments thereof. Two such entities having different specificities are linked using a chemical crosslinking agent conventional in the art. Alternatively, each antibody may be digested to produce F(ab')2 fragments, which may then be reduced to produce individual Fab' fragments. One Fab' fragment may then be derivatized with a reagent and then reacted with the second Fab' fragment of different specificity to regenerate a linkage at the hinge region and create a bispecific F(ab')2 fragment, which is referred to as a heterodimer or oligomer (col. 9, col. 33-60.)

Moreover, Bellet et al. teach that multivalent targets having different epitopes for different binding partners allow for simultaneous binding to the binding partners are known in the art. Bellet et al. in discloses assays for multivalent antigens that have

binding sites for at least two antibodies each against a different epitope on the antigen (col. 2, lines 44-52) wherein the epitopes are sufficiently separated from one another so as to allow simultaneous binding of a different immobilized antibody to each of the epitopes (col. 8, lines 45-61.) It would have been within the skills of the ordinary artisan at the time the invention was made to utilize the Bellet et al. and Ring teachings to modify the Dower et al. invention such that the binding elements for the target have distinct binding specificity by using the chemistries as taught by Ring in a configuration that allows for the simultaneous binding of the two binding elements to the target, as taught by Bellet et al.

As to the limitations regarding the first and second low affinity binding elements being segregated from the third and fourth low affinity binding elements on the solid support, such modifications is suggested by Chin et al. More specifically, Chin et al. teach that thousands of different antibodies can be immobilized in a predetermined order and the targets labeled. Because the antibodies are immobilized in a predetermined order, the identity of the protein captured at each position is therefore known (4, 54- col. 5, line 17.) Many proteins can be simultaneously examined with an array comprising a large umber of immobilized antibodies (col. 6, line 46 – col. 7, line 5.) The skilled artisan would thus be motivated to provide the respective sets of binding affinities for the different targets as discussed above, in an array since Chin et al. teach that this allows for the advantage of simultaneously detecting a large quantity of targets, as would be desirable for convenience. It is understood in the art that in an array, the immobilized elements are separated from each other in spots. Thus, the

skilled artisan would have reasonable expectation of success since the skilled artisan would recognize that in the modification of the Dower reference to detect multivalent target molecules with epitopes having distinct binding specificities to different binding partners/elements, the different binding partners/elements used to identify one type of target molecule is placed in separate spots from the different binding partners/elements used to identify the other type of target molecule.

Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430, in view of Monteforte, 7,091,046.

Dower et al. disclose the invention substantially as claimed (see above), except for the binding elements being distributed randomly on the surface of the support (i.e., such that some binding elements are not distributed in a pattern).

Howevever, Monteforte discloses that molecules may be distributed and identified by position on the solid phase or by virtue of an identifiable or detectable label. The solid phase may be a surface with identifiable loci on its surface or the solid phase may be beads in solution or spread on a support (col. 12, 32-50.) Moreover, using labels such as nanocrystals allow for simultaneous detection (col. 33, lines 17-35). It would have been obvious to the skilled artisan to modify the Dower et al. invention to provide multiple binding elements to detect more than one target, wherein the respective sets of binding elements may be randomly distributed on a surface,

since Montefort discloses that using multiple nanocrystal labels allows for simultaneous detection by detecting the label, i.e., regardless of position on a substrate.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dower et al., 6,465,430, in view of Ring, 5,705,614, and Bellet et al., 5,011,771, and further in view of Chin et al., 6,197,599, as applied to claim 26 above, and further in view of Monteforte, 7,091,046.

Claim 26, from which claim 27 depends, has been discussed above.

for the binding elements being distributed randomly on the surface of the support (i.e., such that some binding elements are not distributed in a pattern).

As to the limitation regarding the random distribution. Monteforte discloses that molecules may be distributed and identified by position on the solid phase or by virtue of an identifiable or detectable label. The solid phase may be a surface with identifiable loci on its surface or the solid phase may be beads in solution or spread on a support (col. 12, 32-50.) Moreover, using labels such as nanocrystals allow for simultaneous detection (col. 33, lines 17-35). It would have been obvious to the skilled artisan to modify the Dower et al. invention to provide multiple binding elements to detect more than one target, wherein the respective sets of binding elements may be randomly distributed on a surface, since Montefort discloses that using multiple nanocrystal labels allows for simultaneous detection by detecting the label, i.e., regardless of position on a substrate.

Response to Arguments

Applicant's arguments filed July 30, 2008 have been fully considered but they are not persuasive.

Applicant asserts the that Dower patent describes a target molecule distributed on and operatively coupled to a support providing an array of a single target molecule, not a plurality of distinct binding elements. Applicant maintains that the binding elements of Applicant's invention do not compete for binding to the target molecule and are distinct binding elements, further contrasting the single target molecule and the plurality of binding element currently claimed.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the binding elements do not compete for binding to the target molecule) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

As to the limitation regarding the binding elements being distinct, this limitation is not recited in the claims other than claims 3, 23 and 24, the claims of which are rejected using the patents to Ring and/or Bellet as secondary reference(s) to address the limitations regarding binding partners (equivalent to Applicant's claimed binding elements) which are distinct as compared to each other. As elaborated above regarding claim 3, it would have been obvious to one of ordinary skills in the art to utilize different binding partners (equivalent to Applicant's binding elements) for

simultaneous binding to the target in the invention disclosed by Dower et al. in the case in which the target is multivalent and has different epitopes for different binding partners, since the skilled artisan would have recognized that the same principle disclosed by Dower et al, that is, using high receptor densities to increase the likelihood of multivalent binding of a molecule to the immobilized receptors, applies also in the case in which the multivalent target molecule has different epitopes for different binding partners, such molecules being disclosed by Bellet et al. With regard to claims 23 and 24, the Ring reference was also used, to show that producing bispecific oligomers with distinct specificities is known in the art. It is noted here that while the Ring reference was utilized in the rejection of claims 23 and 24, the skilled artisan would have recognized that bispecific oligomers need not be used, so long as there are at least two different binding elements, such as the binding partners disclosed by Bellet, as explained in the rejection of claim 3. In other words, the skilled artisan would have recognized that the principle taught by Dower in using high receptor densities to increase the likelihood of multivalent binding of a molecule to the immobilized receptors, apply also to multivalent target molecules with different epitopes for distinct binding elements, whether the binding elements are separate molecules (as is understood to be the case in the Dower reference) or bispecific molecules produced by the methods disclosed by the Ring reference. It is also noted that while it is mentioned above that Applicant argues but does not claim that the binding elements do not compete for binding to the target molecule, it appears that such inclusion in the claims would be obvious to the skilled artisan as well so long as there are target

molecules that bind to different binding partners/elements that do not compete with each other for the same epitope.

Applicant also argues that if two or more different receptors are coupled to a support, then one of skill would not know which receptor is binding which ligand. Applicant states that if a plurality of ligands are coupled to the support, then one of skill would be unable to propagate and enhance the ligands that bind the target receptor as described in the Dower patent. Applicant state that Applicant does not see how one would identify a receptor agonist (the intended purpose of the Dower patent methods) using the teachings of the Dower patent as modified to obviate the current claims, and that such a modification of the Dower patent would render it inoperable providing strong evidence supporting the non-obviousness of the current invention.

These arguments are not persuasive for the following reasons. Where only one type of target molecule is being detected, the two different receptors identify only one target, i.e., the multivalent target molecule that binds to two different, distinct receptors (see discussion of claim 3 above.) Where, for example, two types of target molecules are being detected, simultaneous detection of the two types of target molecules is well known in the art and is explained in the grounds of rejection above (see discussion of claims 23-26.) Specifically, Chin et al. teach that thousands of different antibodies can be immobilized in a predetermined order and the targets labeled. Because the antibodies are immobilized in a predetermined order, the identity of the protein captured at each position is therefore known (4, 54- col. 5, line 17.) Many proteins can be simultaneously examined with an array comprising a large umber of immobilized

antibodies (col. 6, line 46 – col. 7, line 5.) The skilled artisan would thus be motivated to provide the respective sets of binding affinities for the different targets as discussed above, in an array since Chin et al. teach that this allows for the advantage of simultaneously detecting a large quantity of targets, as would be desirable for convenience. It is understood in the art that in an array, the immobilized elements are separated from each other in spots. Thus, the skilled artisan would have reasonable expectation of success since the skilled artisan would recognize that in the modification of the Dower reference to detect multivalent target molecules with epitopes having distinct binding specificities to different binding partners/elements, the different binding partners/elements used to identify one type of target molecule is placed in separate spots from the different binding partners/elements used to identify the other type of target molecule.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Patent Examiner, Art Unit 1641